

### **REMARKS**

In view of the amendments and remarks that follow, Applicants respectfully submit that the application is in condition for allowance. Accordingly, applicants request reconsideration of the application, withdrawal of the rejections of record and issuance of a Notice of Allowance.

Claims 1-20 are pending in the application. Claims 1-19 stand rejected for the reasons of record and Claim 20 has been withdrawn as drawn to a non-elected invention. Claims 11-19 have been canceled and claims 1,2, 4, 5, 7-10 have been amended to put them in condition for allowance. The amendments are not considered to involve the addition of new matter and entry thereof is respectfully requested.

The Office has required restriction of the claims as follows:

Group I - Claims 1-19, drawn to 1,2,4-triazine of formula I, composition and method of use; and

Group II Claim 20, drawn to specific benzamide compounds.

Applicants respectfully affirm their provisional election, without traverse, made during a telephone conversation with the Examiner on August 2, 2004 to prosecute the invention of Group I. Claim 20 has been withdrawn without prejudice to the filing of a divisional application covering said claim.

It is noted and acknowledged that the references cited in the Information Disclosure Statements filed on 11/6/2003 and 11/24/2003 have been made of record.

### **Rejections Under 35 U.S.C. § 112, second paragraph**

Claims 1,2 and 4-19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, in Claim 2, the Office considers the recitation of "and pharmaceutically acceptable salts and prodrugs thereof" to be indefinite. Claim 2 has been amended to be in alternate form and in singular form as requested.

In Claims 1 and 2, the Office notes that the recitation of the term “prodrug” is deemed as indefinite. While disagreeing that the word “prodrug” is indefinite, Claims 1 and 2 and the claims depending therefrom have been amended to delete the term “prodrug” in order to expedite the prosecution of the claims.

In Claims 4,5 and 7-10, the Office notes that the recitation of “at least one of the compounds” renders these claims indefinite. The Office suggests the replacement of this with “one or more”. While disagreeing that “at least one” renders the claims indefinite, the claims have been amended to recite “one or more” in order to expedite the prosecution of these claims.

The Office notes that the recitation of the phrase “including” in claim 11 renders the claim indefinite. However, upon reviewing the claim, the term “including” is not found in the claim. This ground of rejection should be withdrawn.

#### **Rejections Under 35 U.S.C. § 112, first paragraph**

Claims 1, 2 and 4-19 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making prodrugs of the claimed compounds. The Office has summarized the factors to be considered in making an enablement rejection and concluded that the claims are not enabled.

Applicants disagree that the specification does not provide any direction. As noted by the Office, page 11 of the specification provides more than enough direction to one of ordinary skill in this particular art to prepare prodrugs of the compounds of the invention. References are provided showing various forms of prodrugs and their synthesis. Clearly one skilled in the art would be able to use these references and the knowledge in the art to prepare prodrugs of the instantly claimed compounds.

However, while disagreeing with the Office’s conclusion, Claims 1, 2 and 4-19, as noted above, have been amended to delete the term “prodrug” in order to expedite the prosecution of the claims.

Claims 1, 2 and 4-19 are also rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for making salts of the claimed

compounds, does not reasonably provide enablement for making solvates of the claimed compounds.

Applicants disagree that the specification does not provide any direction. Clearly one skilled in the art would be able to use the knowledge in the art to prepare solvates of the instantly claimed compounds.

However, while disagreeing with the Office's conclusion, Claims 1, 2 and 4-19, as noted above, have been amended to delete the term "solvates" in order to expedite the prosecution of the claims.

Claims 11-19 are also rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for treating angiogenesis, does not reasonably provide enablement for treating any proliferative disease, cancer, inflammation, autoimmune disease or "diseases associated with signal transduction pathways operating through growth factor receptors". The Office argues that "the specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The Office goes on to conclude, after considering a number of factors, that undue experimentation would be required to practice Applicants' invention.

While disagreeing with the Office's conclusion, Claims 11-19, as noted above, have been canceled in order to expedite the prosecution of the remaining claims.

#### **Rejections Under 35 U.S.C. § 102**

Claims 1 and 4-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Leftheris et al. WO 02/40486. The Office notes that Leftheris teaches structurally similar pyrrolotriazine compounds. It is noted that in the formula (I) on page 3, all variable groups overlap with those of the instant claims.

Applicants respectfully traverse the rejection and present the following comments. The compounds disclosed in Leftheris et al. differ from the instant compounds in that the instant compounds contain a 1-methylethyl group at the position identified as R<sup>3</sup>Y at the 5-position of the pyrrolotriazine core. This position, identified as R<sup>3</sup> in Leftheris, cannot be anything other than hydrogen, methyl, perfluoromethyl, methoxy, halogen, cyano or NH<sub>2</sub>.

Claim 1 has been amended to add a proviso deleting "methyl" as a potential substituent at the 5-position of the instantly claimed invention. Applicants submit that

Claim 1, as amended, is not anticipated by Leftheris et al. and request that this ground of rejection be withdrawn.

### **Rejections Under 35 U.S.C. § 103**

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leftheris et al. WO 02/40486. The Office notes that Leftheris et al. teaches structurally similar pyrrolotriazine compounds and notes that in the formula (I) on page 3, all variable groups overlap with those of the instant claims. The Office also notes that instant claims 2 and 3 require a specific species while Leftheris et al. differs in not exemplifying these specific compounds.

The Office concludes that it would have been obvious to one having ordinary skill in the art at the time of the invention was made (sic) to make pyrrolotriazine compounds variously substituted with the variables noted as permitted by the reference and expect resulting compounds (i.e., the instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

Applicants respectfully traverse the rejection and provide the following comments. Claim 1 has been amended to add a proviso deleting "methyl" as a potential substituent at the 5-position of the instantly claimed invention. It would not be obvious, in view of the differences between the instant compounds and those disclosed in Leftheris, to prepare the instant compounds. The instantly claimed compounds differ at the 5-position as noted above. Additionally, Leftheris teaches away from the instantly claimed compounds, as shown in Claims 1 and 7, wherein the R<sup>3</sup> substituent is narrowly defined, as well as in any of the preferred structures, all of which include a narrowly defined R<sup>3</sup> substituent that is either methyl, CF<sub>3</sub> or OCF<sub>3</sub>. Applicants submit that Claim 1, as amended, is not anticipated by Leftheris et al. and request that this ground of rejection be withdrawn.

Claims 1 and 4-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-7, 12 and 16 of co-pending Application No. 09/573,829.

Claims 1 and 4-19 are also provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 and 16-25 of co-pending Application No. 10/441,848.

Finally, Claims 1, 2 and 4-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 7-20 of co-pending Application No.10/622,593.

While disagreeing with the provisional rejections, Applicants will consider filing a Terminal Disclaimer upon notification of allowable subject matter.

In view of the foregoing, Applicants submit that the application, as amended, is in condition for allowance and courteously solicit a Notice of Allowance.

If any fee due is not accounted for herein, please charge such fee to Deposit Account No. 19-3880. If any extension of time is required and not petitioned for, such extension is hereby petitioned for, and it is requested that any fee due in connection therewith be charged to the aforementioned Deposit Account.

The foregoing response is believed to be fully responsive to the outstanding Office Action. If a direct personal communication would advance the prosecution of this application, please contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,



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